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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/935,386	08/22/2001	John C. Yu	TSRI 753.1	1866

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EXAMINER	
TON, THAIAN N	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 03/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/935,386	YU, JOHN C.	
	Examiner	Art Unit	
	Thai-An N Ton	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9/02
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicants' Amendments filed 12/19/03 has been considered and entered.

Claims 1-17 are pending and under current examination.

Response to Arguments

The prior rejection of claims 1-10, 12-14 and 17 under 112, 2nd ¶, is withdrawn in view of Applicants' amendments to the claims.

The prior rejection of claims 10-16 under 35 U.S.C. 102(b) as being anticipated by Blair or Steele is withdrawn in view Applicants' arguments, in particular, that the rodent model of Blair does not disclose a rodent model of human leukemia wherein the rodent model has a complement of normal human cells, as required by the claims.

The prior rejection of claims 1-5, 7-9, and 17 under 35 U.S.C. 103(a) in view of Haynesworth and Caplan is withdrawn in view of Applicants' arguments.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *in vivo* mouse models of human leukemia and

methods for making the *in vivo* human leukemia comprising: a) pre-conditioning an SCID mouse by administering to the mouse a sub-lethal dose of irradiation and injecting the mouse with an effective pre-conditioning amount of mononuclear cells obtained from human fetal cord blood; b) maintaining the mouse from step (a) for 5 to 10 days; c) injecting the mouse from step (b) with an effective engrafting amount of primary human leukemia cells; and d) allowing the primary human leukemia cells to engraft in the mouse to produce an *in vivo* model of human leukemia, and methods for making an *in vivo* model of human leukemia comprising: a) pre-conditioning an SCID mouse by administering to the mouse a sub-lethal dose of irradiation and injecting the mouse with an effective pre-conditioning amount of stem cells obtained from bone marrow; b) maintaining the mouse from step (a) for 5 to 10 days; c) injecting the mouse from step (b) with an effective engrafting amount of primary human leukemia cells; and d) allowing the primary human leukemia cells to engraft in the mouse to produce an *in vivo* model of human leukemia, does not reasonably provide enablement for the *in vivo* model of human leukemia as presently claimed, immunodeficient rodents having human fetal cord blood cells and engrafted human leukemia cells, and methods of making the same. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The breadth of the claimed invention is directed to immunodeficient rodents. However, the specification fails to provide an enabling disclosure for such rodents. The specification teaches methods for making *in vivo* models of human leukemia by pre-conditioning immunodeficient rodents by administering a sub-lethal dose of irradiation and injecting the rodent with an effective pre-conditioning amount of mononuclear cells derived from human fetal cord blood, and then injecting the rodent with an effective engrafting amount of primary human leukemia cells. The specification teaches that immunodeficient rodents such as NOD/scid mice would be used in the present invention. See p. 2. The term "rodent" is broad, encompassing mice, squirrels, beavers and rats. See Encyclopædia Brittanica. The specification states that, "Numerous immunodeficient rodent models as known in the art." However, the specification fails to provide specific teachings with regard to immunodeficient rodents, other than NOD/scid mice and the implementation of the invention only animals lacking an immune system in totality would permit the growth of the engrafted human leukemia cells. Animals such as nude mice and rats would not permit engraftment of xenogeneic bone marrow because, while these animals lack T-cells, their B-cell capability would mount sufficient immune response. Furthermore, at the time of filing only SCID mice could be found in the art, and the specification provides no guidance as to obtaining SCID animals of other species. For example, http://www.taconic.com/anmodels/animlmod.htm provides description of traditional immunodeficient rat and mouse models.

Particularly, they state that NIH Nude (athymic) rats exhibit deficient T cell activity with lymph nodes and Peyer's patches showing lymphocyte depletion in T-lymphocyte-dependent regions. With regard to NOD/scid mice, they state that the experience a block in T and B-cell lymphocyte development. Thus, the art supports the availability of SCID mice with a total lack of an immune response; however, the art fails to provide teachings with regard to the breadth of the claims, immunodeficient rodents. If Applicants feel that the breadth of immunodeficient rodents is enabled, Applicants are invited to specifically point to evidence to the contrary.

Accordingly, in view of the lack of teachings or guidance provided by the specification with regard to the utilization of immunodeficient rodents, for the breadth claimed, other than the exemplified NOD/scid mice in the claimed methods, the art recognized teachings that only animals that lack an immune response would permit the engraftment of xenogeneic bone marrow, and the lack of teachings or guidance with regard to the breadth of the claims encompassing immunodeficient rodents, and the availability in the art on only scid mice, it would have required undue experimentation for one of skill in the art to make and/or use the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 10-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Yu *et al.* [**Proceedings of the Am. Association for Cancer Research Annual Meeting**, March 1999, Vol. 40, page 660, Abstract No. 4352].

The claims are directed to an immunodeficient rodent having human fetal cord blood cells and having engrafted human leukemia cells.

Yu teaches the sub-lethal irradiation, pre-conditioning of immunodeficient NOD/scid mice with fetal cord blood mononuclear cells, and the subsequent engraftment of human T-ALL [T-cell acute lymphoblastic leukemia] cells. It was found that cells that were recovered from the mouse bone marrow and spleen resembled the original patient's cells.

Accordingly, Yu anticipate the claimed invention.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Thaian N. Ton whose telephone number is (571) 272-0736. The Examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time), with alternating Fridays off. Should the Examiner be unavailable, inquiries should be directed to Amy Nelson, Acting SPE of Art Unit 1632, at (571) 272-0804. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

TNT

Thaian N. Ton
Patent Examiner
Group 1632

DEBORAH CROUCH
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